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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/079,609	02/21/2002	Stefan Kochanek	50125/020002	7269

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/079,609	KOCHANEK ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/23/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *7,8,11-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10,21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Final Rejection

Claims 1-25 are pending.

Applicants' traversal, the amendment to claims 1-6, 10, and 21, and the addition of claims 22-25 in paper filed 7/23/04 is acknowledged and considered.

Election/Restrictions

An iris pigment epithelial cell in claim 2 and claims 7, 8, and 11-20 and an anti-angiogenetic factor, anti-oxidative factor, lysosomal factor, vasodilating factor in claim 3 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and GDNF, NGF, BDNF, CNTF, bFGF or neurotrophin 3, neurotrophin 4, and neurotrophin 5 in claim 3 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/20/03.

Claim Objections

Claim 25 is objected to because of the following informalities: the phrase "a pigment epithelial cell of the eye as claimed in claim 1" on lines 1-2 is grammatically incorrect for a dependent phrase. Suggest amending the phrase to recite: -- the pigment epithelial cell of the eye as claimed in claim 1 --. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The intended use of the genetically modified pigment cell of the eye (e.g., in a fixed assemblage of cells) in the instant claim 6 does not have patentable weight for prior art rejections. See MPEP 2111.02. An intended use does not provide a structural difference between the claimed invention and the prior art.

The intended use of the genetically modified pigment cell of the eye (e.g., medicament or diagnostic aid) in the instant claim 21 does not have patentable weight for prior art rejections. See MPEP 2111.02. An intended use does not provide a structural difference between the claimed invention and the prior art.

The intended use of the genetically modified pigment cell of the eye (e.g., where the cell has been cultivated in the presence of a feeder layer or in serum free-medium) in the instant claims 23 and 24, respectively, does not have patentable weight for prior art rejections. See MPEP 2111.02. An intended use does not provide a structural difference between the claimed invention and the prior art.

Claims 1, 2, 3, 4, 5, 6, 9, and 21 remain and claims 22-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Kovesdi et al., (US 2003/0045498). Kovesdi teaches administering an adenoviral vector comprising a nucleic acid sequence encoding a pigment epithelium-derived factor (PEDF) to retinal pigment epithelial cells (abstract, pages 2, 3, 4, 6, 15, and 16). Kovesdi teaches that the adenoviral vector is deficient in genes essential for viral replication such that the vector can accept large inserts of exogenous DNA (pages 4-5). Kovesdi teaches that any promoter can be used in the vector, e.g., constitutive, regulatable, tissue-specific (pages 6-7). Kovesdi teaches a pharmaceutical composition comprising the vector and using the vector to study treatment of ocular disorders (pages 12 and 13).

Applicant's arguments filed 7/23/04 have been fully considered but they are not persuasive.

Applicants argue that Kovesdi does not satisfy the standard for anticipation because it fails to disclose an adenoviral vector with large DNA capacity and it is stated in the specification, at page 6, line 14-15, that "an adenoviral vector of large DNA capacity is understood by the skilled worker to be adenoviruses which comprise no viral coding DNA sequences."

The argument is not found persuasive because the statement in the specification is not a special definition as asserted by applicants because the statement is a general statement made by the applicants. The claims read on any adenovirus that can accept large inserts of exogenous DNA, e.g., gutless, second generation, etc. In addition, as noted in MPEP 2111 claims are given their broadest interpretation consistent with the specification. It is proper to use the specification to interpret what the applicant meant by a word or phrase recited in the claim. However, it is not

proper to read limitations appearing in the specification into the claim when these limitations are not recited in the claim.

Claims 1, 2, 4-6, 9, and 21-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Baffi et al. (IOVS, pages 3302-GB128, cited on a PTO-1449). Baffi teaches human retinal pigment epithelial cells comprising a second-generation adenoviral comprising a promoter operatively linked to a B-gal gene.

Claims 1, 2, 4-6, 9, and 21-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Reichel et al. (Ophtalmologe, 96:570-577, 1999 (English translation of article in German) and cited on a PTO-892). Reichel teaches gene transfer into retinal pigment epithelium (RPE) (page 3). Reichel teaches using adenovirus for gene transfer in the eye, wherein the adenovirus has gene regulated by a promoter (pages 7-8 and 10). The adenovirus lacks all viral genes (page 8).

Claim Rejections - 35 USC § 103

The e following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi et al., (US 2003/0045498) taken with Tezel et al., (Exp. Eye Res. (1998) 66, 807-815).

Kovesdi teaches administering an adenoviral vector comprising a nucleic acid sequence encoding a pigment epithelium-derived factor (PEDF) to retinal pigment epithelial cells (abstract, pages 2, 3, 4, 6, 15, and 16). Kovesdi teaches that the adenoviral vector is deficient in genes essential for viral replication such that the vector can accept large inserts of exogenous DNA (pages 4-5). Kovesdi teaches that any promoter can be used in the vector, e.g., constitutive, regulatable, tissue-specific (pages 6-7). Kovesdi teaches a pharmaceutical composition comprising the vector and using the vector to study treatment of ocular disorders (pages 12 and 13). However, Kovesdi does not specifically teach culturing the genetically modified retinal pigment epithelial cell (RPE) of the eye in serum-free media.

However, at the time the invention was made, Tezel teaches that serum-free media can be used for culturing RPE cells (page 807). Tezel further teaches culturing the cells onto tissue-culture plastic pre-coated with bovine corneal endothelial extracellular matrix (page 807). Tezel teaches, "The presence or absence of serum-derived hormones, cytokines, carrier proteins, cell attachment factors and cell spreading factors can have a profound effect on the behavior of RPE cells in tissue culture and may mask the specific effects of a particular exogenous cytokine(s) on RPE. For these reasons, several researchers have cultured RPE with reduced or not serum supplementation (page 807)." "This is particularly important for RPE, because RPE cells exhibit phenotypic heterogeneity (page 812)."

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Kovesdi taken with Tezel to culture genetically modified retinal pigment epithelial cells in serum-free media. One of ordinary skill in the art would have been motivated to culture the RPE cells in serum-free media because Tezel teaches that culturing RPE cells in serum free medium avoids the effect of hormone, cytokines, carrier proteins, cell attachment factors and cell spreading factors on the behavior of RPE cells in tissue culture.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 7/23/04 have been fully considered but they are not persuasive for the reason set forth under the 102(e) prior art rejection.

Claims 1 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi et al., (US 2003/0045498) taken with Funk et al., (US 6,667,176) in further view of Williams et al., (Nature, 1988, 336:684-7).

Kovesdi teaches administering an adenoviral vector comprising a nucleic acid sequence encoding a pigment epithelium-derived factor (PEDF) to retinal pigment epithelial cells (abstract, pages 2, 3, 4, 6, 15, and 16). Kovesdi teaches that the adenoviral vector is deficient in genes essential for viral replication such that the vector can accept large inserts of exogenous DNA (pages 4-5). Kovesdi teaches that any promoter can be used in the vector, e.g., constitutive, regulatable, tissue-specific (pages 6-7). Kovesdi teaches a pharmaceutical composition comprising the vector and using the vector to study treatment of ocular disorders (pages 12 and 13). However, Kovesdi does not specifically teach culturing the genetically modified retinal pigment epithelial (RPE) cell of the eye in the presence of a feeder layer.

However, at the time the invention was made, Williams teaches that maintenance of stem-cell phenotype in vitro requires the presence of a feeder layer (page 684).

In addition, at the time the invention was made, Funk teaches that RPE cells are progenitor cells (column 17, lines 34-57).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Kovesdi taken with Williams and Funk to culture genetically modified retinal pigment epithelial cells in the presence of a feeder layer. One of ordinary skill in the art would have been motivated to culture the RPE cells in the presence of a feeder layer because Williams teaches that culturing stem cells in the presence of a

feeder layer maintains stem-cell phenotype *in vitro* and Funk teaches that RPE cells are progenitor cells.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 7/23/04 have been fully considered but they are not persuasive for the reason set forth under the 102(e) prior art rejection.

Claims 1 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi et al., (US 2003/0045498) taken with Funk et al., (US 6,667,176) and Williams et al., (Nature, 1988, 336:684-7) in further view of Tezel et al., (Exp. Eye Res. (1998) 66, 807-815).

Kovesdi teaches administering an adenoviral vector comprising a nucleic acid sequence encoding a pigment epithelium-derived factor (PEDF) to retinal pigment epithelial cells (abstract, pages 2, 3, 4, 6, 15, and 16). Kovesdi teaches that the adenoviral vector is deficient in genes essential for viral replication such that the vector can accept large inserts of exogenous DNA (pages 4-5). Kovesdi teaches that any promoter can be used in the vector, e.g., constitutive, regulatable, tissue-specific (pages 6-7). Kovesdi teaches a pharmaceutical composition comprising the vector and using the vector to study treatment of ocular disorders (pages 12 and 13). However, Kovesdi does not specifically teach culturing the genetically modified retinal pigment epithelial (RPE) cell of the eye in a serum-free medium and in the presence of a feeder layer.

However, at the time the invention was made, Williams teaches that maintenance of stem-cell phenotype in vitro requires the presence of a feeder layer (page 684). In addition, Funk teaches that RPE cells are progenitor cells (column 17, lines 34-57).

Furthermore, at the time the invention was made, Tezel teaches that serum-free media can be used for culturing RPE cells (page 807). Tezel further teaches culturing the cells onto tissue-culture plastic pre-coated with bovine corneal endothelial extracellular matrix (page 807). Tezel teaches, "The presence or absence of serum-derived hormones, cytokines, carrier proteins, cell attachment factors and cell spreading factors can have a profound effect on the behavior of RPE cells in tissue culture and may mask the specific effects of a particular exogenous cytokine(s) on RPE. For these reasons, several researchers have cultured RPE with reduced or not serum supplementation (page 807)." "This is particularly important for RPE, because RPE cells exhibit phenotypic heterogeneity (page 812)."

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Kovesdi taken with Williams and Funk in further view of Tezel to culture genetically modified retinal pigment epithelial cells in serum-free medium and in the presence of a feeder layer. One of ordinary skill in the art would have been motivated to culture the RPE cells in the presence of a feeder layer because Williams teaches that culturing stem cells in the presence of a feeder layer maintains stem-cell phenotype *in vitro* and Funk teaches that RPE cells are progenitor cells. In addition, one of ordinary skill in the art would have been motivated to use serum-free medium in the method because Tezel teaches that culturing RPE cells in serum free medium avoids the effect of hormone, cytokines,

carrier proteins, cell attachment factors and cell spreading factors on the behavior of RPE cells in tissue culture.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 7/23/04 have been fully considered but they are not persuasive for the reason set forth under the 102(e) prior art rejection.

Conclusion

Applicant's amendment and Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 7/23/04 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i) and MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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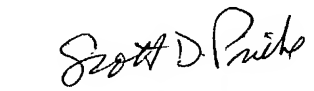

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